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The Epidemiology and Management of Severe Hypertension

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ORIGINAL ARTICLE

The epidemiology and management of severe hypertension

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Hypertension guidelines stress that patients with severe hypertension (systolic blood pressure (BP) ⩾180 or diastolic BP ⩾110 mm Hg) require multiple drugs to achieve control and should have close follow-up to prevent adverse outcomes. However, little is known about the epidemiology or actual management of these patients. We retrospectively studied 59 207 veterans with hypertension. Patients were categorized based on their highest average BP over an 18-month period (1 July 1999 to 31 December 2000) as controlled (<140/90 mm Hg), mild (140–159/90–99 mm Hg), moderate (160–179/100–109 mm Hg) and severe hypertension. We examined severe hypertension prevalence, pattern, duration, associated patient characteristics, time to subsequent visit, percentage of visits with a medication increase, and final BP control and antihypertensive medication adequacy. Twenty-three per cent had ⩾1 visit with severe hypertension, 42% of whom had at least two such visits; median day with severe hypertension was 80 (range 1–548). These subjects were significantly older, more likely black, and with more comorbidities than other hypertension subjects. Medication increases occurred at 20% of visits with mild hypertension compared to 40% with severe hypertension; $P<0.05$). At study end, 76% of patients with severe hypertension remained uncontrolled; severe hypertension subjects with uncontrolled BP were less likely to be on adequate therapy than those with controlled BP (43.7 vs 45.4%). Among hypertensive veterans, severe hypertension episodes are common. Many subjects had relatively prolonged elevations, with older, sicker subjects at highest risk. Although, follow-up times are shorter and antihypertensive medication use greater in severe hypertension subjects, they are still not being managed aggressively enough. Interventions to improve providers' management of these high-risk patients are needed.

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Introduction

Hypertension is among the most prevalent chronic conditions worldwide; with rates as high as 70% among adults in developed countries such as Poland.[1] Although hypertension is usually asymptomatic, it may be associated with considerable morbidity and mortality. The higher the blood pressure (BP), the greater the risk for adverse outcomes including development of coronary artery disease, congestive heart failure, stroke and kidney disease.[2] Hypertension treatment has been clearly shown to reduce this risk.[2–4]

Accordingly, the current World Health Organization/International Society of Hypertension and the European Society of Hypertension guidelines and the prior Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC) guidelines classify BP into grades or stages based on the absolute BP level.[5–7] Although absolute cardiovascular risk is based not only on BP levels, but associated cardiovascular risk factors or target organ damage, individuals with the highest levels, grade/stage[3] or severe hypertension (that is, systolic BP ⩾180 mm Hg or diastolic BP ⩾110 mm Hg)[5,8] have a 20–30% 10-year risk of cardiovascular disease, that increases to very high risk, >30%, in the presence of any risk factors or target organ damage.[5] Further, these subjects are also at high short-term risk for serious cardiovascular events, the risk increasing with the degree and speed of elevation. Because of this, guidelines also stress that such patients should have close follow-up with reassessment at most within 1 week, and will require multiple drugs to achieve control.[5,9,10]

Although much has been written about the epidemiology and management of the general hypertension population, relatively little is known about these issues in those with severe hypertension. Limited cross-sectional data suggest a prevalence among those with hypertension in the

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8–19% range.[10–13] How long such patients are exposed to high BPs, or how they are being managed in actual practice is relatively unknown, with existing data based on small samples and select populations.[12–14]

The purpose of the present study was to examine the following issues with respect to patients with severe hypertension: (1) what is the epidemiology of severe hypertension, in terms of prevalence, pattern of severe hypertension and duration of severe hypertension? (2) what patient characteristics are associated with severe hypertension? (3) how are patients with severe hypertension being managed in everyday practice, including time to next visit, percentage of visits with a medication increase and number of BP medications by final BP control?

Materials and methods

Study population

The study population is previously described.[15] Briefly, we identified individuals with hypertension who were receiving regular outpatient care at geographically diverse sites within the largest integrated health-care system in the United States, the Veterans Health Administration (VA), using the VA's National Patient Care Database (NCPD) through 2000, eligible subjects: (1) had at least two NPCD-listed hypertension diagnoses, ICD-9-CM code 401, between 1 July 1997 and 30 June 1999; and (2) were regular VA users (that is, $\geqslant 3$ NPCD-listed visits to a general medicine or subspecialty medical clinic between 1 July 1999 and 31 December 2000). Subjects were followed from 1 July 1999 through 31 December 2000. The study protocol was approved by the Bedford VA Hospital's institutional review board.

Data collection

Data sources were the Veterans Health Information Systems and Technology Architecture (VISTA), that is, the VA's electronic record system, the NPCD and Medicare files. VISTA, maintained at each site, contains multiple files including clinical data such as vital signs, laboratory results, pharmacy records and provider notes. (We previously found the vitals file very complete with provider notes contributing minimal additional BP information.)[16] VISTA also contains diagnoses and procedure information from all outpatient visits and inpatient stays, which is transferred to a central data repository and incorporated into the NPCD.[17]

Demographics and comorbidities were obtained from the NPCD (1998 to 2000 inclusive), supplemented by Medicare denominator, inpatient and outpatient files (MEDPAR, Carrier and Outpatient files). We used the Medicare denominator file as our primary race source because this is patient identified and supplemented this with VA race data. Baseline comorbidities were identified by the presence of specified ICD-9-CM codes in the 12 months preceding and including the index visit.[15] Height, weight and BP were obtained from VISTA vitals, and medications from VISTA pharmacy files (1 July 1999 to 31 December 2000).

Analyses

Available BPs were averaged at each visit. All visits during 1 July 1999 through 31 December 2000 were categorized according to the average systolic and diastolic BPs as follows: controlled ($<$140/90 mm Hg), mild (140–159/90–99 mm Hg), moderate (160–179/100–109 mm Hg) and severe ($\geqslant$180/110 mm Hg) hypertension. Patients were then grouped based on their visit with the highest average BP category unless otherwise specified. If systolic and diastolic BPs fell into different categories, the higher category was used. Among patients with more than one severe hypertension episode, patient level analyses considered only the first episode unless otherwise indicated.

Objective 1: examine the epidemiology of patients with severe hypertension. We first determined the prevalence of severe hypertension in our cohort based on the number of subjects who had at least one visit with severe hypertension divided by the total sample of hypertension patients. We also looked at the proportion of all visits with severe hypertension and the median number of visits with severe hypertension per patient. Next, we characterized the pattern of severe hypertension by determining the following proportions: (1) those who had a single visit with severe hypertension, with no severe hypertension at the next visit (that is, an isolated spike in their BP); (2) those who had severe hypertension at two or more consecutive visits (persistent severe hypertension); (3) those who had an intervening visit with a lower BP but then another visit with severe hypertension (recurrent severe hypertension). We further determined the median number of recurrences per patient. In addition, we examined time in days to a subsequent visit with a BP $<$180/110 mm Hg as a proxy for the duration of (that is, exposure to) severe hypertension, and compared among severe hypertension groups. We summed these time periods for patients with recurrent episodes. (This was examined first by censoring subjects with no visit after the severe hypertension visit at either the last day of the study period or death, and then by excluding them.)

Objective 2: patient characteristics associated with severe hypertension. We next compared patients with severe hypertension to subjects without severe hypertension, grouped by highest BP category, with respect to age, gender, race, baseline comorbidities (including cardiovascular risk factors and pre-existing cardiovascular conditions, and Charlson

index),[18,19] body mass index (BMI). We also compared severe hypertension subgroups with respect to these same characteristics.

We used χ^2-analysis for categorical variables, and *t*-tests, one-way analysis of variance (ANOVA) with Tukey's multiple comparison procedure, or Wilcoxon rank-sum tests as appropriate for continuous variables.

As part of a sensitivity analysis, we repeated objectives 1 and 2 assigning subjects to BP categories based on the first visit of the study period.

Objective 3: examine the management of patients with severe hypertension. We next examined actions potentially under clinician control. The following analyses were carried out at the visit level: (1) we determined the time in days to the next visit that included a BP assessment following a visit with severe hypertension. We used Wilcoxon rank-sum tests to compare the median interval to the next visit among severe hypertension subgroups, and between visits with severe hypertension to visits with moderate hypertension, mild hypertension or controlled BP. (2) We then examined the percentage of visits associated with a medication increase. To determine medication increases at a visit, we defined baseline medication use based on the 6-month period preceding study entry (that is, we examined medication data out to 1 January 1999); using methods we previously developed, a patient was considered to have an increase at a given visit if the dose of an existing medication was increased or a new medication was started.[20,21] We compared the proportion of visits with a medication increase among the severe hypertension subgroups then compared among visits with moderate, mild hypertension or controlled BP using χ^2-tests. We also looked at the impact of this increase on BP control at the subsequent visit for the severe hypertension group.

Although we lacked information on specialty referrals for BP management or to exclude secondary hypertension, as a proxy, we examined differences in proportions of patients seen in subspecialty clinics at which BP management might be addressed by χ^2-analysis and generating 95% confidence intervals. These clinics included hypertension, renal, cardiology and endocrinology clinics. We further looked at the frequency of these visits with a primary diagnoses related to hypertension (ICD-9-CM codes 401, 402, 403, 404 and 405 (secondary hypertension)) and the frequency of any 405 code at these visits.

To examine medication use and BP control at study end, we then categorized subjects based on their highest average BP at a visit before the last study visit. We compared the percentage of patients who achieved a BP $<140/90$ mm Hg at the last study visit by BP group. We next compared BP groups by mean number of prescribed antihypertensive medications (using ANOVA), percentage of subjects on each major class of antihypertensive medication and the percentage on adequate therapy defined as a regimen containing at least three different classes of drugs at least one of which had to be a loop or thiazide diuretic[9] at the last study visit using χ^2-tests. We then examined the mean number of prescribed antihypertensive medications at the time of the last visit by prior highest BP category and final BP control (that is, BP $<140/90$ mm Hg; yes/no) using linear regression models, comparing both within BP groups, and across groups for controlled vs uncontrolled. We also repeated analyses comparing among severe hypertension subgroups. Finally, we examined adequacy of antihypertensive therapy at the last study visit and final BP control. Within each BP group defined by the highest BP before the last study visit, we used χ^2-tests to examine likelihood of adequate therapy at study end by final BP control (yes/no); we also compared adequacy across BP categories. We performed similar comparisons among severe hypertension groups.

Results

Objective 1

Our total sample consisted of 59 207 subjects. The mean age was 65 years: 58% were white and 97% were men.[15] Twenty-three per cent ($N=13\,735$) had at least one visit with severe hypertension; among these subjects the median number of such visits was 1 (range 1–57). Six per cent of all visits (21 992/325 105) were associated with severe hypertension. Of note, 87% of visits with a BP of $\geqslant 180/110$ mm Hg had only one BP documented on the day of the visit.

Of the severe hypertension group, 18% had severe hypertension at two or more consecutive visits (persistent), 23% had one or more intervening visits with a lower BP but then another visit with severe hypertension (recurrent); 58% had a single visit with a BP $\geqslant 180/110$ mm Hg (isolated spike). In 17% of subjects with an isolated spike, there was no subsequent documented visit. The median number of recurrences among the severe hypertension group was 0, range 0–34 (interquartile range 0–1). The median number of days with severe hypertension overall was 80 (range 1–548; Table 1) and varied

Table 1 Total exposure to severe hypertension

BP category	*Exposure to severe hypertension Days, median (range)*[a]
Severe hypertension, overall	80 (1–548)
Persistent	182 (2–548)
Recurrent	103 (2–534)
Isolated spike	50 (1–549)

Abbreviation: BP, blood pressure.
[a]Significant difference with respect to number of days exposed between groups ($P<0.001$).

Table 2 Baseline patient characteristics by highest BP group

Characteristic	*Controlled* N = *5170*	*Mild* N = *19 290*	*Moderate* N = *21 012*	*Severe* N = *13 735*
Age, mean (s.d.), years	63.7 (11.3)	63.8 (11.2)	65.5 (10.9)	67.0 (10.8)[a]
Gender, female, no. (%)	121 (2.3)	516 (2.7)	604 (2.9)	453 (3.3)[a]
Race, no. (%), white	3988 (77.1)	14 563 (75.5)	15 573 (74.1)	9545 (69.5)[a]
Black	659 (12.8)	2,842 (14.7)	3,741 (17.8)	3302 (24.0)[a]
Hispanic	71 (1.4)	233 (1.2)	300 (1.4)	153 (1.1)
Others	108 (2.1)	358 (1.9)	341 (1.6)	221 (1.6)
Unknown	344 (6.7)	1294 (6.7)	1057 (5.0)	514 (3.7)[a]
BMI, mean (s.d.), $kg\,m^{-2}$	28.8 (5.4)	29.4 (5.5)	29.5 (5.8)	29.2 (6.1)[a]
Comorbidities				
Cerebrovascular disease, no. (%)	669 (12.9)	2261 (11.7)	2781 (13.2)	2305 (16.8)[a]
Congestive heart failure, no. (%)	1055 (20.4)	2338 (12.1)	2354 (11.2)	1814 (13.2)[a]
Coronary artery disease, no. (%)	2392 (46.3)	6998 (36.3)	7128 (33.9)	4802 (35.0)[a]
Diabetes, no. (%)	1584 (30.6)	5841 (30.3)	6996 (33.3)	5263 (38.3)[a]
Hyperlipidaemia, no. (%)	2563 (49.6)	8927 (46.3)	8895 (42.3)	5151 (37.5)[a]
Peripheral vascular disease, no. (%)	532 (10.3)	1688 (8.8)	2141 (10.2)	1760 (12.8)[a]
Renal disease, no. (%)	340 (6.6)	1050 (5.4)	1378 (6.6)	1430 (10.4)[a]
Tobacco use, no. (%)	503 (9.7)	1897 (9.8)	1951 (9.3)	1219 (8.9)[a]
Charlson index, mean (s.d.)	1.3 (1.4)	1.2 (1.2)	1.2 (1.2)	1.4 (1.3)[a]

Abbreviations: BMI, body mass index; s.d., standard deviation.
[a]$P<0.05$ for among-group comparisons and pair-wise comparisons; the severe hypertension group was significantly different than the three other hypertension groups with respect to all the characteristics listed. However, with respect to race, the prevalence of Hispanics in the severe hypertension group was only significantly different compared to the moderate hypertension group.

significantly by severe hypertension subgroup. (Overall exposure did not change significantly if we excluded subjects with a single visit.)

Categorizing subjects using the first study period visit, 7% of subjects had severe hypertension, of whom 27% had persistent, 28% had recurrent and 45% had an isolated spike. Exposure trends were similar.

Objective 2

Compared to subjects with lower BPs, severe hypertension subjects were older, ($67.0 + 10.8$ vs $64.6 + 11.2$ years; $P<0.05$), were more likely to be black (24 vs 16%; $P<0.05$) and women (3.3 vs 2.7%, $P<0.05$) compared to all other subjects combined ($N = 45\,472$). They also had more total comorbidities (for example, Charlson index $1.4 + 1.3$ vs $1.2 + 1.2$, $P<0.05$) and a higher prevalence of specific comorbidities such as diabetes, renal disease and peripheral vascular disease; although when further divided into BP categories, the controlled BP group had the highest prevalence of coronary artery disease, congestive heart failure and hyperlipidaemia. (See Table 2 for comparisons among BP categories.)

Among severe hypertension subgroups, the recurrent and persistent were similar with respect to age and race distribution, but the recurrent had the most comorbidities followed by the persistent then the isolated spike group. The isolated spike group was younger and more likely to be white (see Table 3). Similar trends were seen when subjects were categorized by the first study visit (data not shown; available from authors).

Objective 3

The median time to a subsequent visit after presentation was 42 days (range 1–503) for severe hypertension, 52 days (1–513) for controlled BP, 60 days (1–518) for mild and 55 (1–496) for moderate hypertension visits ($P<0.05$ for between-group differences).

Hypertension medication increases occurred at 40% of severe hypertension, 10% of controlled, 20% of mild and 32% of moderate hypertension visits ($P<0.05$). Among visits with severe hypertension, medications were increased at 41% of visits with severe hypertension among the persistent group, 36% of the recurrent group and 42% of the isolated spike group ($P<0.05$). If a medication was increased at a given visit with severe hypertension, BP was controlled 13.2% of the time at the next visit, versus 12.5% of next visits if there was no medication increase. (This difference was not significant (NS)).

The proportion of patients seen in a subspecialty clinic at which BP management might be addressed not surprisingly tended to increase with increasing BP category, and was significantly higher in the severe hypertension group (except for cardiology clinic visits) presumably in part driven by the higher prevalence of renal disease or diabetes in the more severe group (Table 4). The frequency of such visits associated with a primary diagnosis of hypertension ranged from 6.2% among the controlled group, 8.9% of the mild, 13.3% of the moderate, to 20.0% among the severe hypertension group. In severe hypertension subgroup, this ranged from 17.5% among the isolated spike group, 18.0% among the recurrent group and 29.8% among the persistent group ($P<0.5$

Table 3 Baseline patient characteristics by severe hypertension group

Characteristic	*Persistent severe* N = *2517*	*Recurrent severe* N = *3210*	*Isolated spike* N = *8008*
Age, mean (s.d.), years	67.4 (10.8)	67.7 (10.6)	66.6 (10.9)[a]
Gender, female, no. (%)	80 (3.2)	104 (3.2)	269 (3.4) NS
Race, no. (%), white	1631 (64.8)	2144 (66.8)	5770 (72.1)[a]
Black	734 (29.2)	910 (28.4)	1658 (20.7)[a]
Hispanic	26 (1.0)	42 (1.3)	85 (1.1)
Others	40 (1.6)	40 (1.3)	141 (1.8)
Unknown	86 (3.4)	74 (2.3)	354 (4.4)[a]
BMI, mean (s.d.), $kg\,m^{-2}$	29.2 (6.1)	29.0 (6.1)	29.4 (6.1)[a]
Comorbidities			
Cerebrovascular disease, no. (%)	470 (18.7)	612 (19.1)	1223 (15.3)[a]
Congestive heart failure, no. (%)	350 (13.9)	490 (15.3)	974 (12.2)[a]
Coronary artery disease, no. (%)	834 (33.1)	1217 (37.9)	2751 (34.4)[a]
Diabetes, no. (%)	1064 (42.3)	1396 (43.5)	2803 (35.0)[a]
Hyperlipidaemia, no. (%)	912 (36.2)	1178 (36.7)	3061 (38.2)[a]
Peripheral vascular disease, no. (%)	323 (12.8)	514 (16.0)	923 (11.5)[a]
Renal disease, no. (%)	291 (11.6)	465 (14.5)	674 (8.4%)[a]
Tobacco use, no. (%)	211 (8.4%)	287 (8.9%)	721 (9.0) NS
Charlson index, mean (s.d.)	1.4 (1.3)	1.6 (1.4)	1.3 (1.3)[a]

Abbreviations: BMI, body mass index; NS, not significant; s.d., standard deviation.
[a]$P<0.05$ for among-group comparisons and pair-wise comparisons; recurrent and persistent groups were similar with respect to age, white and black race distribution, BMI, prevalence of cerebrovascular disease, congestive heart failure, diabetes and hyperlipidaemia.

Table 4 Percentage of patients with subspecialty clinic visits[a]

Highest BP category	*Hypertension clinic % (95% CI)*	*Renal clinic % (95% CI)*	*Cardiology clinic % (95% CI)*	*Endocrinology clinic % (95% CI)*	*Any subspecialty clinic*[b] *% (95% CI)*
Controlled ($N=5170$)	0.2 (0.1–0.4)	0.6 (0.4–0.8)	9.0 (8.2–9.8)	1.5 (1.2–1.7)	10.6 (9.8–11.5)
Mild ($N=19\,290$)	0.3 (0.2–0.4)	0.9 (0.8–1.1)	8.6 (8.2–9.0)	1.6 (1.4–1.8)	10.8 (10.3–11.2)
Moderate ($N=21\,012$)	0.4 (0.3–0.5)	1.7 (1.5–1.8)	8.6 (8.2–8.9)	1.9 (1.7–2.1)	11.5 (11.1–12.0)
Severe ($N=13\,735$)	0.8 (0.7–1.0)	3.7 (3.4–4.0)	8.9 (8.4–9.4)	2.2 (2.0–2.5)	14.1 (13.6–14.7)
Persistent ($N=2517$)	1.2 (0.9–1.7)	4.6 (3.8–5.5)	7.2 (6.3–8.3)	2.5 (1.9–3.1)	13.7 (12.4–15.1)
Recurrent ($N=3210$)	1.0 (0.7–1.4)	6.2 (5.4–7.1)	11.7 (10.6–12.8)	2.8 (2.3–3.4)	19.4 (18.0–15.1)
Isolate spike ($N=8008$)	0.7 (0.5–0.9)	2.4 (2.1–2.7)	8.3 (7.8–9.0)	2.0 (1.7–2.3)	12.2 (11.5–12.9)

Abbreviations: BP, blood pressure; CI, confidence interval.
Non-overlapping of CIs indicates the proportions (percentages) are significantly different from each other.
[a]Clinics at which hypertension is likely to be treated.
[b]Any subspecialty clinic: hypertension, renal, cardiology or endocrinology.

for between-group differences). The frequency of a code for secondary hypertension ranged from 0% among endocrinology visits, 0.1% for cardiology, 0.9% for renal, to 2.8% of all hypertension clinic visits.

When categorized by the highest available BP before the last visit of the study, at the end of study 24% of the severe hypertension group had controlled BP, compared to 73% of the controlled, 51% of mild and 33% of the moderate group ($P<0.05$). For the severe hypertension subgroups, the isolated spike group was most likely to be controlled (27%), followed by the recurrent (21%) and the persistent groups (16%; $P<0.05$ for between-group differences). (Of note, 1390 subjects with only one visit with a BP were excluded from this analysis; 500 had controlled, 525 had mild, 243 had moderate and 122 (9%) had severe hypertension. We found similar results to those reported below if we included these subjects in analyses and assumed they had an additional visit and their BP category was stable (data not shown; available from authors).)

At the end of study, the mean number of BP medications increased significantly with increasing BP category (Table 5; Figure 1). In addition, severe hypertension patients were significantly more likely to be on all classes of antihypertensives compared to the other groups (Table 5). Among severe hypertension subgroups, the persistent and recurrent subgroups were on more medications at study end than

Table 5 Medication use at study end by highest preceding BP category

Characteristic	*Controlled* N = *6428*	*Mild* N = *19 488*	*Moderate* N = *19 528*	*Severe* N = *12 373*	*Persistent* N = *2264*	*Recurrent* N = *2678*	*Isolated spike* N = *7431*
No. medications, mean (s.d.)	2.0 (1.1)	2.1 (1.1)	2.3 (1.2)	2.8 (1.4)[a]	3.2 (1.5)	*3.2 (1.5)*	2.6 (1.3)[a]
ACEIs/ARBs, no. (%)	3167 (49.3)	9525 (48.9)	10 193(52.2)	7121 (57.6)[a]	1400 (61.8)	1548 (57.8)	4173 (56.2)[a]
α-Blockers, no. (%)	1196 (18.6)	3952 (20.3)	4438 (22.7)	2980 (24.1)[a]	572 (25.3)	688 (25.7)	1720 (23.2)[a]
β-Blockers, no. (%)	2201 (34.2)	5797 (29.8)	5836 (29.9)	4494 (36.3)[a]	934 (41.3)	1056 (39.4)	2504 (33.7)[a]
CCBs, no. (%)	1912 (29.7)	6536 (34.1)	7765 (39.8)	5760 (46.6)[a]	1142 (50.4)	1333 (49.8)	3285 (44.2)[a]
Diuretics, no. (%)	2503 (38.9)	7595 (39.0)	8383 (42.9)	5980 (48.3)[a]	1161 (51.3)	1346 (50.3)	3473 (46.7)[a]
Other vasodilators, no. (%)[b]	173 (2.7)	548 (2.8)	938 (4.8)	1527 (12.3)[a]	421 (18.6)	479 (17.9)	627 (8.4)[a]
Adequate therapy, no. (%)[c]	1519 (23.6)	4608 (23.7)	6018 (30.8)	5457(44.1)[a]	1197 (52.9)	1383 (51.6)	2877 (38.7)[a]

Abbreviations: ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; BMI, body mass index; CCBs, calcium channel blockers; s.d., standard deviation.
[a]$P<0.05$ for among-group and pair-wise comparisons; analyses were carried out separately for the BP groups and severe hypertension subgroups. In pair-wise comparisons, for BP groups, the mean number of medications and the percentage on each medication class or on adequate therapy increased with increasing BP group, except for β-blocker use where the controlled group was more likely to be on a β-blocker than the mild or moderate group. Also, the controlled and mild groups were not significantly different with respect to ACEI/ARB use, diuretic use, other vasodilators use and percentage on adequate therapy. For the severe hypertension subgroups, the mean number of medications, the percentage on each medication class or adequate therapy was significantly lower for the isolated spike group than the persistent or recurrent, except for ACEI/ARB use which was similar to the recurrent. The persistent and recurrent groups were similar in all comparisons except for ACEI/ARB use.
[b]Includes clonidine, hydralazine, methyldopa and minoxidil.
[c]Adequate therapy: a regimen containing at least 3 different classes of drugs at least one of which is diuretic.

the isolated spike subgroup (Table 5; $P<0.05$ for between-group differences). The proportion on each medication class was significantly lower for the isolated spike group than the persistent or recurrent group, except for ACEI/ARB use which was similar to the recurrent group (Table 5). Despite a trend towards higher use of each medication class among the persistent group compared to the recurrent, the differences were not significant.

Across all BP groups, those with controlled BP at study end (<140/90 mm Hg) were on more medications than those with uncontrolled BP (although this difference was not significant for the severe hypertension group; Figure 1). Within severe hypertension subgroups, the mean number of medications at study end was only significantly different between controlled and uncontrolled subjects for the isolated spike group (Figure 1).

Use of three or more medications including a diuretic at the last visit increased by increasing preceding highest BP category (although the difference between the controlled and mild groups was not significant) (see Table 5 and Figure 2). Among the severe hypertension subgroups, those with persistent or recurrent elevations were more likely to be on adequate multi-drug therapy compared to the isolated spike group (Table 5). Similar to the medication class analysis, the proportions on adequate therapy in the persistent and recurrent groups were not significantly different (Table 5).

When examining adequacy of therapy and final BP control, subjects with uncontrolled BP at the last visit were less likely to be on adequate multi-drug therapy than those with controlled BP within any given BP group or severe hypertension subgroup (Figure 2), although differences were not significant for the severe hypertension group (45.4 vs 43.7%, NS; Figure 2). In subgroups, differences were only significant among the isolated spike subgroup (Figure 2).

Discussion

This is the largest study to date examining the epidemiology and management of patients with severe hypertension. This is also the first to characterize the pattern of severe hypertension, to examine management of such patients and to compare among hypertension categories. We found that severe hypertension is relatively common, with almost one quarter of subjects having at least one visit with severe hypertension. Further, in many cases this represented more than a single isolated spike, with over 40% having persistent or recurrent severe elevations.

Factors associated with severe hypertension were similar to those found in previous studies of poor BP control. Subjects with severe hypertension were older, more likely to be black, women, and had more medical comorbidities than subjects with lower BPs.

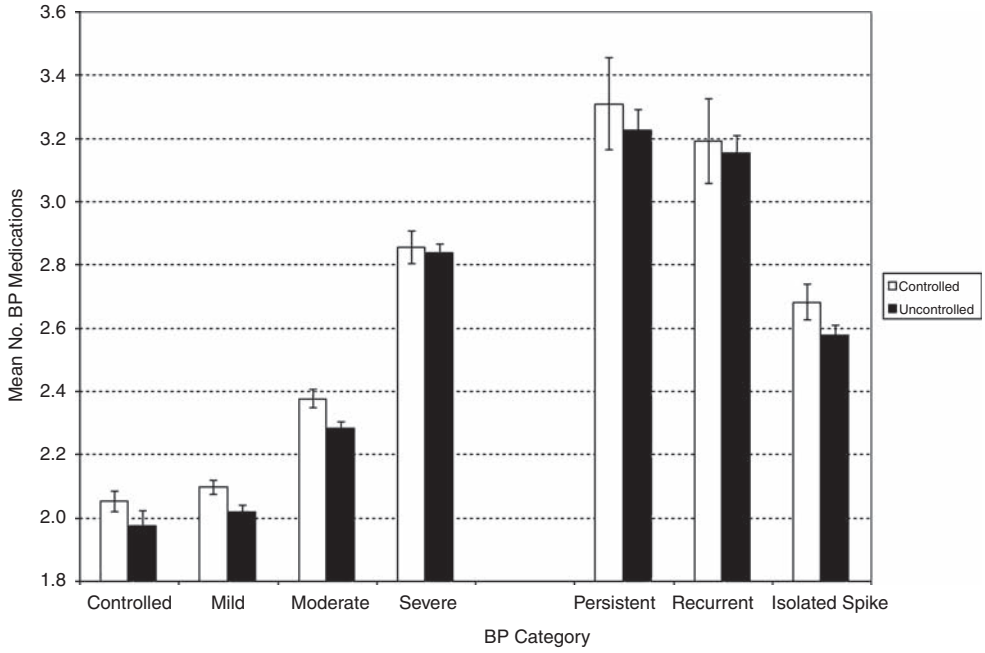

Figure 1 Mean number of antihypertensive medications at study end by highest preceding blood pressure (BP) category and final BP control. Means shown with surrounding bars representing 95% confidence intervals. (Error bars overlap for those in the controlled BP group with controlled vs uncontrolled BP at study end. However, by Student's *t*-test, the means of controlled vs uncontrolled are significantly different, $P<0.05$.)

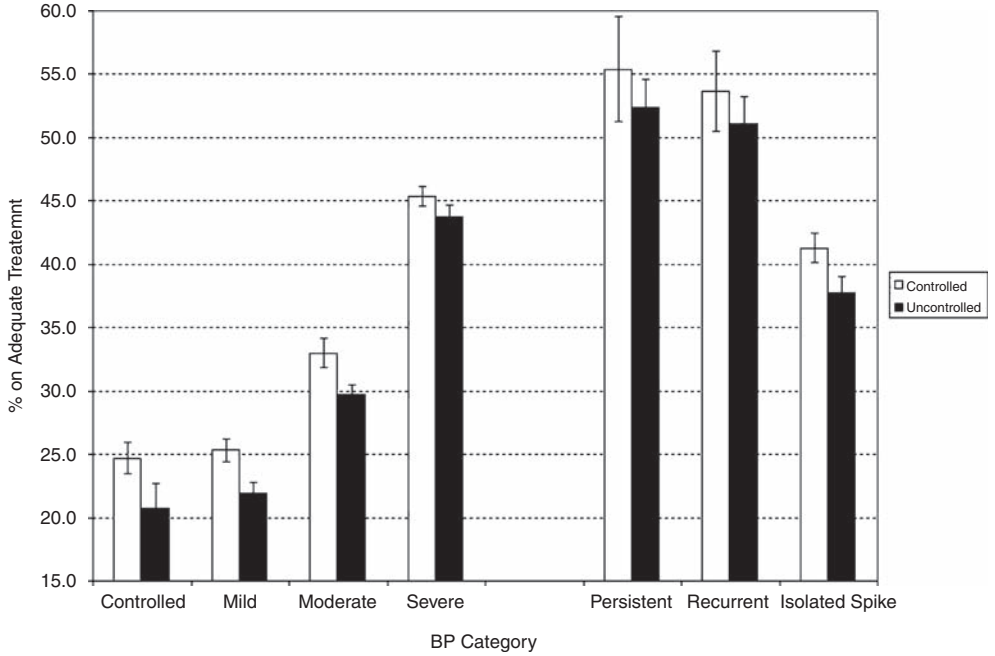

Figure 2 Adequacy of blood pressure (BP) treatment at study end by highest preceding BP category and final BP control. Bars represent 95% confidence intervals.

Similarly, among those with severe hypertension, those with recurrent or persistent elevations were older and women. The recurrent group had more medical comorbidities than those with persistent elevations or the isolated severe group. Analyses of National Health and Nutrition Examination Survey data likewise found age and being black were associated with poorer control.[22,23] An analysis of data from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial, additionally

found being woman, having diabetes and an elevated creatinine were associated with lack of control at follow-up.[24] We found similar associations in our previous examination of factors associated with poor BP control in this sample.[15]

We also found that patients with severe hypertension are often not treated aggressively enough. The median follow-up time after a visit with severe hypertension was 42 days, which is much longer than the guideline-recommended interval. Although medications were more likely to be increased as the severity of BP category increased, this still occurred at less than 50% of visits with severe hypertension and many subjects with severe hypertension remained uncontrolled at the end of the study. Although mean number of medications increased by BP category, within any category, including the severe hypertension group, subjects with uncontrolled BP at study end tended to be on fewer medications than controlled subjects. Further, a significant percentage of the severe hypertension group were not on adequate therapy at study end and continued to have poorly controlled BP. Among the severe hypertension subgroups, those on more medications tended to be better controlled at study end. Subjects with persistent severe hypertension were more likely to have their medications increased but were slightly less likely to be controlled compared to the recurrent group.

Existing data specifically examining severe hypertension epidemiology and management are very limited, being based on small populations and select samples. The largest observational study examined outcomes in 142 emergency room (ER) patients presenting with BPs $\geqslant$220 mm Hg systolic or $\geqslant$120 mm Hg diastolic.[12] Among those treated as urgencies and discharged from the ER, the mean time to a follow-up appointment was 21 days. Thirty percent of subjects returned to the ER with uncontrolled hypertension, 14% with hypertensive complications, within an average of 33 days. Drug management was also only examined in the acute ER setting. Longer-term use of drugs, BPs and clinical outcomes were not tracked. A cross-sectional Spanish study assessing cardiovascular risk and comorbidities in hypertension patients attending primary care practices found the following prevalences of BP categories among 1413 subjects: controlled 3%, mild 50%, moderate 39%, severe 8%.[13] The mean age of their sample was similar to ours at 65.3 (11.4) years. Among high-risk patients (based on comorbidities and absolute BP levels) there was no medication change in 30%. No information is given about the severe hypertension subjects as a distinct group. Only one study specifically examined subjects with severe hypertension.[12] Lalljie and Lalljie[12] studied management and BP outcomes in 48 subjects with severe hypertension of 252 (19%) patients presenting to a Jamaican hypertension specialty practice. Follow-up data were only reported on 31 of these subjects, of whom more than 50% achieved BP control during up to 2 years of follow-up with most requiring at least four drugs. Unlike our study, subjects were younger (62% were $<$65 of age), more likely to be women, with lower baseline comorbidity rates (31% had diabetes, 21% had heart failure and 15% had coronary artery disease).

This study has a few caveats. It was performed in a sample of predominantly male veterans with relatively high disease burden and good access to medical care and medications. Therefore, findings may not be generalizable to other settings. Our data predate VA quality performance data that show improvement in control rates over time, such that the current prevalence of severe hypertension is likely lower.[25] However, given the prevalence of hypertension in the VA population has increased from 37% in 1999 to 55–60% in 2006 (based on ICD-9 codes), in absolute numbers this still likely represents many patients with severe hypertension.[26] We lack data on some management aspects of severe hypertension subjects that may be of interest such as referrals to hypertension specialists (although we do know that less than 1.0% of these patients were seen in a hypertension clinic) or investigations to exclude secondary hypertension.

We have also demonstrated that the method used to define the BP group, for example, highest average BP at any visit vs the first visit of the 18-month study period produces dramatically different values with respect to severe hypertension prevalence. Further deviation from the true prevalence may result because BPs were obtained from the vitals file, with only one BP available for almost 90% of visits; we may be missing BPs present in provider notes. In addition, we cannot exclude white coat hypertension because we do not have access to home BP measures or 24 h ambulatory blood pressure monitoring. However, in a previous study, we found that provider notes contributed minimal additional BP information beyond the vitals file, including rare documentation of ambulatory or home BPs.[16]

Our examination of hypertension management was based on highest BP as opposed to the first study BP because we wanted to determine providers' responses to such high BPs. JNC 7, published after our study, emphasizes that most patients will require more than one antihypertensive drug to achieve control.[9] In our study using data through the end of 2000, the majority of patients across all BP groups were already on at least two medications, with many also on a diuretic. Thus, we would not expect substantially different findings with more current data other than slightly lower rates of severe hypertension as noted above. Our measure of treatment adequacy does not account for medication dosage and thus may be overestimating treatment adequacy. It is possible that this may in part explain

the lack of statistical difference between the proportions controlled and uncontrolled in the severe hypertension group at study end. However, this still does not account for the fact that many subjects in the severe hypertension group were not even on adequate therapy based on number of medications.

Although BP control, especially in severe hypertension subjects, may be improved by treatment intensification, specialist referral and investigation for and management of secondary causes of hypertension, we were unable to examine reasons for lack of treatment intensification and lacked data on referrals to hypertension specialists (although we do know that less than 1.0% of these patients were seen in a hypertension clinic) or on investigations to exclude secondary hypertension. Other investigators have found clinical uncertainty about true BP values to be a prominent reason for lack of treatment intensification.[27] Whether this has a role in patients with such high BPs is unclear.

In conclusion, among veterans with hypertension, severe BP elevations are relatively common with many patients having persistent or recurrent elevations with inadequate follow-up and intensification of therapy. This suggests that clinical inertia is not just an issue among those with mildly elevated BP. Given the increased cardiovascular risk associated with this degree of BP elevation, there is a need for better understanding of how these patients are being managed. In addition, interventions are needed to overcome clinical inertia and improve providers' management of hypertension, especially regarding severe hypertension.

What is known about the topic

- Little data on prevalence and management of patients with severe hypertension.
- Prevalence estimates of 8–19% based on small sample sizes ($N = 252$–1413) in select populations (for example, patients referred to hypertension clinics).
- No data on patterns of severe hypertension and how long patients are exposed to such high BPs.

What the study adds

- Largest study to date examining prevalence and management of patients with severe hypertension ($N = 59\,207$, of whom 13 735 had at least one visit with severe hypertension).
- First to characterize the pattern of severe hypertension, that is, isolated spike vs persistent or recurrent.
- First to compare management of patients with severe hypertension to patients with other categories of hypertension.

Conflict of interest

This project was funded in part by the Department of Veterans Affairs Health Services Research and Development service grant number SDR 99-300-1 and by Bristol-Myers Squibb. Dr Berlowitz has served as a consultant for Bristol-Myers Squib. All aspects of design, conduct and analysis were under sole authority of the authors without any restriction on publication.

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